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Review Article

A SYSTEMATIC REVIEW OF *OREOSYCE AFRICANA* HOOK.F. (FAMILY-CUCURBITACEAE) PLANT PROFILE, BIOACTIVITIES AND CHEMICAL CONSTITUENTS

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ABSTRACT

Attempts to wipe out the mosquito vector, which have been pursued for many years with synthetic insecticides is compromised by increased mosquito resistance to insecticides and use of inorganic insecticides raises environmental toxicity concerns. Due to public and user concerns of synthetic insecticides, plant product has become an important component in organized mosquito control and becoming widely accepted by many authorities including the World Health Organization. Therefore, *Oreosyce africana* as plant-based biodegradable insecticides would be used as alternatives to synthetic mosquitocides for the control of mosquito. *Oreosyce africana* was used for many ailments, ranging from anti-malarial to anti-gonorrhea treatment and anthelminthic. The qualitative phytochemical analysis of *O. africana* crude extracts is known to possess bioactive characteristics. The *O. africana* purified fractions had the most potent mosquitocidal active components with potency of impregnated nets lasted for two months. The structural elucidations of the active ingredients in the fractions were determined using a combination of ^{1}H- ^{13}C-NMR, DEPT-135 and GC-MS measurements. This revealed the presence of linoleic acid (9, 12-Octadecadienoic acid (Z,Z)- as the major chemical constituent in the first fraction and similar analysis of second fraction showed the presence of dibutyl phthalate as the major chemical constituent and both have proven insecticidal effects. Since the majority of populations at high risk of contracting malaria live in rural areas, insecticidal plants were used in Ethiopia for malaria control. This review is based from the perspective of traditional insecticidal properties of *O. africana* for their mosquitocidal efficacy, phytoconstituents and to promote traditional methods of mosquito control.

KEYWORDS: Biological activity, Cucurbitaceae, Mosquitocide, *Oreosyce africana*, Phytochemicals.

1. INTRODUCTION

According to World Health Organization report more than 80% of the world's population still depends on traditional medicines for their health security.[1] Thus plants may serve as a potential source for novel insecticidal compounds, which is becoming more widely accepted by many authorities including the WHO as a viable vector control. Medicinal plants are rich in a wide variety of secondary metabolites and are valuable source of novel biologically active molecules; and several studies have confirmed the insecticidal activities of natural products from plant origin.[2,3]

Malaria is by far the most important mosquito-transmitted human disease. Malaria transmission in Ethiopia depends substantially on the major vector, *Anopheles arabiensis*, which is prevalent across all malarious areas in Ethiopia.[4,5] The vector is endophilic and endophagic in most localities with exophilic tendencies in certain instances. Of malaria control methods the control of the mosquito vector is usually the most effective and desirable. Malaria mosquito control intervention has been applied in the country since the 1950s. The types of control efforts have changed with time. However, the greatest challenge facing larviciding programs is that the *Anopheles* mosquito has a long flight range and, therefore, all sites within two to three kilometers of the community need to be sprayed.[6] The general control is based mainly on adult mosquito control measures by insecticides.[7]

In the 1950s and 1960s governments in many countries organized programs of indoor house spraying (IRS) with insecticides, especially DDT. However, this was expensive to maintain and mosquitoes became resistant to DDT. Resistance of the vector to DDT reduces the overall effectiveness of IRS.[8] Modern pyrethroid

insecticides work better than DDT; however the widespread use of pyrethroids (deltamethrin, permethrin, cypermethrin) for long lasting insecticide treated nets and IRS in recent years for malaria control efforts, leading to the development of resistance in mosquitoes in the regions where the insecticides are used have been reported.[9,10,11,12,13,14]

One of the significant gains in insect control was due to chemicals which brought the hope that unwanted insect populations would be significantly diminished. However, due to increasing the resistance of mosquitoes to synthetic insecticides with a new awareness of environmental contamination caused by overuse of chemical insecticides, and an increased chemical cost,[15] has necessitated development of new control strategies and our interest in natural or botanical insecticides has been revived.

Despite no historical record confirms as to when the plant origin compounds came into use for insect vector control, tobacco, pyrethrum and rotenoids have been in use since 1763, early to middle of 19th century and 1848, respectively.[16] Global utilization of medicinal plants has increased enormously over the last four decades.[17] It has been estimated that 14-28% of higher plant species are used medicinally and that 74% of pharmacologically active plant derived components were discovered after following up on the traditional uses of medicinal plants.[18]

A study, conducted by Abebe[19] described that the techniques and processes employed in the collection and preparations of traditional medicine are simple and do not take a lot of time, which makes it generally cheaper than the synthetic medicine.[20] Also described that the screening of locally available medicinal plants for mosquito control would create local employment, reduce dependence on expensive imported products and stimulate local efforts to enhance public health.

Ancient peoples used smoke from burning cattle or goat dung to drive out mosquitoes from their caves or huts before sleeping. Later on, the application of mosquitocidal plants for the control of mosquitoes is recommended[21] because they minimize the accumulation of harmful residues in the environment due to their biodegradability and hence plant products against mosquito vectors indicated as possible alternatives to synthetic chemical mosquitocides.[22]

In Ethiopia, like other developing countries, medicinal plants have been used as remedies for many years and still are used for the treatment of different ailments. But, for malaria elimination to be compatible with the development efforts that are currently underway; it needs to be controlled by using an integrated application of vector control interventions including potent mosquitocides from plant sources. So, chemical insecticides must be augmented by affordable and environment friendly local plant products for maximum reduction in vector longevity and hence transmission, which are in use among the different peoples and regions of the country.[23,24,25]

However, the application of plant derivatives for larvicides and adulticides to malaria vector control is uncommon in Ethiopia. This review is, therefore, focuses on the traditional uses, malaria vector control and phytochemistry of *O. africana*. Furthermore, due to rapid increase in population and accelerated rate of urbanization a number of plant species are under increased threat of extinction. This increase in rate of extinction of species and the consequent reduction of potential medicinal plants constitutes a major environmental concern that requires urgent attention. It is therefore important to review this species resource and assess their potentials and define strategies to conserve them.

1.1. Distribution of *Oreosyce africana*

Oreosyce africana Hook.f. (Cucurbitaceae) is slender climber or trailer growing to 3 m (MANABASI, local native language in Afan Oromo and Amharic). The *O. africana* specimen was collected from Akakai and Ilu Gelan districts.[26,27] Voucher specimens of *O. africana* Hook.f. (DB.18) has been collected and type specimen authenticity confirmed by taxonomic experts at the Department of Plant Biology and Biodiversity Management and deposited at the National Herbarium of Ethiopia, Addis Ababa University for further reference. Its habitat is in wet or moist *Aningeria- Syzygium* forest margins, grassland and in plantations at altitude between 1650-2000 m asl.[28] It is native to Ethiopia but also found in Angola, Burundi, Cameroon, Kenya, Madagascar, Malawi, Rwanda, Tanzania, Uganda, Zaire, Zambia, and Zimbabwe.[29] Another study by[30] also reported that *O. africana* is found in South Africa.

1.2. Taxonomic classification of *Oreosyce africana*

Table 1: Taxonomic hierarchy of *Oreosyce africana*.[31]

Kingdom	**Plantae**
Subphylum	Euphyllophytina
Infraphylum	Radiatopses
Subclass	Magnoliidae
Superorder	Rosanae
Order	Cucurbitales
Family	Cucurbitaceae
Genus	*Oreosyce*
Species	*O. africana* Hook.f.

Figure 1: Picture of *Oreosyce africana* (Photograph: by Damtew Bekele, 2012)

2. Traditional uses of *Oreosyce africana*

Traditional herbal medicine is accessible, uses locally available plants, is relatively cheap and is very personal. In many countries in the Tropics including Ethiopia, people have little access to modern medicine. The family Cucurbitaceae contributes higher number of medicinal species in Ethiopia.[32,33,24,34] The leaf part of *O. africana* is used as an anthelminthic for intestinal worms and its leaf also used as medicine for a burned part.[35] In south-east Tanzania, traditional medical practitioners make the boil of *O. africana* with the vegetable gruel for pregnant women to drink which helps makes the birth easy and they also rub themselves with its leaves against trichophytosis.[29] The filtrate obtained from *O. africana* was reported to be given through hypodermal injection using a syringe to treat gonorrhea.[34,36]

The insecticidal properties of plants have been used in Ethiopia, where plant materials are easily available and their use in health practices is a tradition. According to,[37] a study by[26] showed the people in Akaki district (east-central Ethiopia) traditionally used *O. africana*'s powder of crushed leaves by sprinkling for mosquito management and control of cattle ticks and other arthropod pests. In another study, *O. africana* was used for anti-malarial treatment.[38]

The medicinal plants reported for the prevention and control of malaria vector and for the other healthcare use is a good indicator of the potential that exists locally so long as scientific procedure is added to the indigenous knowledge.[25]

3. Bioactivities of *Oreosyce africana*

The uses of plant materials for insecticides compared with many synthetic insecticides have a relatively low mammalian toxicity, a short period of activity, and a fairly broad spectrum of control,[39,40] reported that the 80% methanol crude leaf extract of *O. africana* exhibited potent mosquitocidal activities (LC_{50} 18.74 and LC_{90} 39.66 ppm) against *An. arabiensis*. The mortality of *An. arabiensis* with *O. africana* extract was relatively higher than among the others at lower concentrations which is the best insecticide because less quantity is needed.[40] This was a confirmation of the ethnobotanical information provided for its use as an insecticide against various ectoparasitic pests on cattle.[26] In view of the high mosquitocidal activity of the crude extract, a further chemical investigation on *O. africana* was carried out. Phytochemical studies on *O. africana* have afforded several types of compounds such as alkaloids, phenols and saponins.[40,41] Among the different metabolites screened from plants, extracts containing alkaloids, saponins, terpenoids and triterpenes have been demonstrated to have profound insecticidal activity.[42,2] The demonstration of phytochemical secondary metabolites in *O. africana*, whose crude extracts caused high mortality to adult mosquitoes, was a further indicator of insecticidal active compounds.[43,2]

The dichloromethane fraction of *O. africana* contained constituents with demonstrable adulticidal activity.[44] It is to be expected that since different phytochemical constituents dissolve in specific solvents.[45,44] Also noted that purified fractions of *O. africana* (leaf extract)

possess a very high adulticidal effect against *An. arabiensis*. It can be considered as effective adulticide based on WHO standards as it produces >60% mortality against the adult stages of the malaria vector *An. Arabiensis.*[46] Data from *O. africana* leaf extracts against *An. arabiensis* showed converse relationship between extract efficacy and solvent polarity where efficacy increased as polarity decreases.[47] Also reported that showed decline in mortality of mosquitoes with increasing solvent polarity of a mosquitocidal plant extract. Moreover,[2] described that the bioactivity of phytochemicals against mosquito can vary significantly depending on plant species and solvent used in extraction.

The isolates from the leaves extract of *O. africana* produce a broad spectrum of insecticidal and other biological activity. The larvicidal effect of dichloromethane fraction of *O. africana*, of which linoleic acid is the major component, is proof to its broad spectrum of bioactivity. Furthermore, the broad spectrum of bioactivity of linoleic acid is evident from its inhibition of parasitemia in mice infected with *Plasmodium vinckei* and *Plasmodium yoelii* in a 4-day suppressive test[48,49] had reported that linoleic acid isolated from *Ricinus communis* has insecticidal activity against *Spodoptera frugiperda* (Noctuidae). The extracts of *Annona squamosa* and *Annona muricata* (Annonaceae) contained linoleic acid against adults of *Aedes albopictus* and *Culex quinquefasciatus* had significant insecticidal effects compared to mortality induced by deltamethrin.[50]

The selected plant extracts are used for adulticide and it also be used for larvicide against *An. arabienis.* According to,[51] the active purified fractions of *O. africana* designated as fraction IV had the most potent larvicidal active components against *An. arabiensis* among the fractions tested (LC_{50} of 2.507 and LC_{90} of 7.721 ppm) at 24 hr post-exposure and showed significant differences at $p<0.05$. The plant product is good evidence to consider the methyl 9,12-heptadecadienoate containing products identified from *O. africana* for the larvicides in malaria control and elimination effort currently in place. A study by[52] showed the benzene crude extract of *Citrullus vulga*ris leaves (Cucurbitaceae) to have an LC_{50} value of 18.56 ppm and LC_{90} value of 39.08 ppm against *An. stephensi* larvae.

Specific evidence for linoleic acid, the chemical compound identified as larvicide in this study, as a larvicide exists from *Citrullus colocynthis* (L.) Schrad (Cucurbitaceae) with an LC_{50} value of 9.79 ppm and LC_{90} value of 37.42 ppm against fourth instar larvae of *An. stephensi* Liston.[53] Another study by[54] also described that *Citrullus colocynthis* constituted a mixture of fatty acids which had the mosquito larvicidal activity. Exploiting the natural interactions between fungi and nematodes, linoleic acid was discovered to be the nematicidal principle by which nematode-trapping fungi kill the prey.[55] Linoleic acid was isolated from submerged cultures in which the formation of traps was induced by nematodes. It exhibited nematicidal activity at 5 μg/ml towards *Caenorhabditis elegans.*

Two purified fractions of *O. africana*, purified using preparative thin-layer chromatography had the potent adulticidal activities against *An. arabiensis* with an LC_{50} of 2.206 and LC_{90} of 7.811 ppm and with an LC_{50} of 2.62 and LC_{90} of 11.779 ppm at 24 hrs post-exposure, respectively.[56] Chemical investigations of *O. africana* leaves extract led to the isolation two major chemical constituents, which showed a relatively strong mosquitocidal activity. The structural elucidation of the active ingredients using GC-MS analysis showed the presence of 9,12-Octadecadienoic acid (Z,Z) as the major chemical constituent (98.35%) in the first fraction and dibutyl phthalate as the major chemical constituent (97.75%) in the second fraction.

The chemical components of the second fraction also have been reported to possess insecticidal bioactivities. When used as a solvent, dibutyl phthalate is in oil-soluble dyes, insecticides, peroxides and other organic compounds (European Chemicals Agency (ECHA),[57]). Dibutyl phthalate and permethrin impregnated clothing provides good protection against chigger mite - the vectors of scrub typhus.[58] Therefore, it is possible that the compounds from *O. africana* could synergistically or independently cause mosquitocidal effects.

The enhanced adulticidal activity of purified fractions of *O. africana* compared to their respective crude extracts and partially purified extracts showed that purification of plant extracts would significantly improve the bioefficacy of the active constituents in an extract. Accordingly, the HPLC method enabled assessment of the levels of the active components of *O. africana* extract purified fractions, first and second, obtained from preparative TLC.[56] Many plant defensive metabolites have clearly demonstrated mechanisms of insecticidal.[59,60] reported one of the main chemical constituent of *Citrullus colocynthis* Linn. (Cucurbitaceae) is linoleic acid.[61] Also proved the isolation and identification of linoleic acids from *Citrullus colocynthis*. The adulticidal activity of linoleic acid containing product in the first fraction, on cage bioassay against *An. arabiensis* with residual activity persisting for up to two months,[56] is a promising discovery in view of the reported decline after two to four months in the residual activity of permethrin, the commonly used synthetic insecticide for mosquito net impregnation.[62,63] Furthermore, the existence of evidence for organic insecticides such as Azadiracthin[64] as a replacement for inorganic/synthetic insecticides, is a good indication for considering the linoleic acid and dibutyl phthalate containing products identified from *O. africana* in the present study.

Today, only a few percent of the population produces the agricultural products needed for our industrialized society. However, recently the Ethiopian Science and Technology Ministry has initiated a preliminary study on indigenous medicinal plants knowledge so as to identify, describe, document and disseminate the existing indigenous knowledge in the country. Therefore, new strategies are constantly being developed to produce high yield and high-quality plant products. Perhaps the brightest future for specializing in plant products will be using *O. africana* extracts that was found to be effective in the small scale industries and their efficiently control the malaria mosquito by organized vector control agencies.[65] described the most economically important of the natural plant compounds used in commercial insect control. Education of the user is also necessary and is best achieved through both the efforts of the producers and county extension agents. The products of *O. africana* are expected to be patented and it is believed that these results will benefit most agricultural nations.

Environmental concern and natural resource development programs have necessitated the utilization of appropriate technological and management techniques in an integrated approach to bring about an effective degree of vector suppression. Therefore, plant derived insecticides will minimize the problem of induction of resistance in the mosquito population and their environmental benefits considerable which will apparently continue to render the extracts effective for a long time as malaria mosquito control agents.

Table 2: Bioactivities of *Oreosyce africana.*

Parts used	Reported activity	References
Leaves	Anti-trichophytosis	[29]
Leaves	Anthelminthic	[35]
Whole plant	Anti-malaria	[38]
Root	Anti-gonorrhoea	[34]
Leaves	Anti-gonorrhoea	[36]
Leaves	Anti-mosquito/Anti-pest	[26]
Leaves	Mosquitocidal	[40]
Leaves	Mosquito adulticidal	[41][44][56]
Leaves	Mosquito larvicidal	[51]

3.1. Isolated compounds of *Oreosyce africana*

According to the report of,[56] the chromatography of the dichloromethane extract of leaves of *O. africana* were further separated by preparative thin layer chromatography yielded biological active fractions and the structure of the compound was determined by spectroscopic means (^{1}H- and ^{13}C-NMR, DEPT and GC-MS) and upon comparison with the reported spectral data (Figure 2-4).

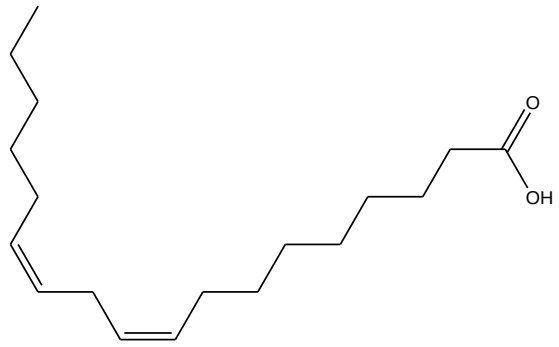


Figure 2: Chemical structure of a 9,12-Octadecadienoic acid (Z,Z)- compound in the first fraction isolated from *O. africana* leaves.

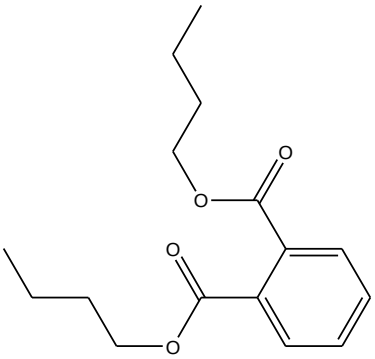
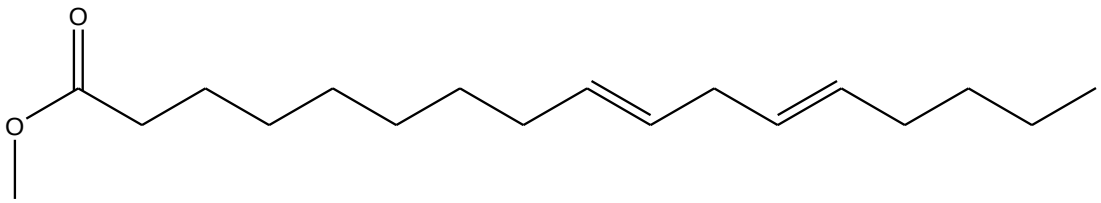


Figure 3: Chemical structure of dibutyl phthalate in the second fraction isolated from *O. africana* leaves.

The NMR spectral analysis in combination with the GC-MS of fraction IV was determined to be methyl 9,12-heptadecadienoate which is in agreement with linoleic acid whose structure is depicted in Figure 4.



methyl 9,12-heptadecadienoate

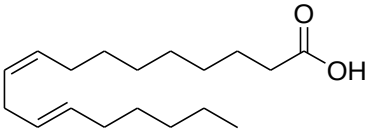


Figure 4: Chemical structure of methyl 9,12-heptadecadienoate and linoleic acid, respectively.

4. CONCLUSIONS

It is desirable to use bioactive plants as alternative agents for the control of mosquitoes as they are locally available, potentially less expensive, they can be propagated easily and sustainable, biodegradable and have a low environmental impact. Moreover, the plant products utilized as mosquitocides can provide a useful tool to promote localized control of persistent malaria. The promising effect of purified fraction I and II isolated by preparative thin layer chromatography and fraction IV of *O. africana* isolated by using flash column chromatography for the control of mosquito adults as they pronouncedly enhanced the mortality of mosquito with the treatment. Therefore, compounds from *O. africana* such as (9, 12-Octadecadienoic acid (Z,Z)-, dibutyl phthalate and methyl 9,12-heptadecadienoate have a potential to be developed as an effective alternative to conventional synthetic insecticides for the control of *An. arabiensis.* This review showed that the use of indigenous medicinal plant based products by individual and communities can provide as a prophylactic measure for protection against various mosquito-borne diseases in combination with the ongoing anti-vector interventions.

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